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REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Claim 1 has been amended to include the features of previous claims 10, 11, 17 and 18. Claims 10, 11, 17 and 18 have been canceled without prejudice or disclaimer. No new matter has been added. Claims 1-8 and 12-16 are pending.

Claim rejections - 35 U.S.C. § 103

Claims 1-8, 10-18 are rejected under 35 USC 103(a) as being unpatentable over US 4,275,031 (Fischer et al.) in view of US 5,374,561 (Pugia). Applicants respectfully traverse the rejection.

Claim 1 requires the test piece for creatinine measurement to include a compound expressed by the formula (1) and a transitional metal or its salt that forms a colored complex with the compound, the transitional metal being Pd(II). The test piece required by claim 1 can be used to evaluate the presence or absence of creatinine and to determine the amount of creatinine in a sample based upon the degree of inhibition of the colored complex formation by creatinine (see page 3, lines 7-12 of the specification).

Fischer is directed to a cuvette (also referred to as an "agent") for carrying out a colorimetric or photometric determination (col. 2, lines 14-15). The cuvette includes a molded support, reagents for colorimetric or photometric determinations, and organic polymers (col. 2, lines 16-20). The reagents are applied to the molded support, such that the reagents are embedded in the organic polymers (col. 1, lines 50-51). The reference teaches that the material from which the moldings are made must be of such nature that no reagents are absorbed therein or held fast thereto (col. 3, lines 13-15). The reference further notes that non-absorbent refers, inter alia, to non-absorption of the embedded reagents, and distinguishes their support from the prior art by noting that absorbent supports, such as are customarily used for reagent strips, cannot be used (col. 3, 16-19). The reference also teaches that their cuvette can be used for determinations of specific substances, including inorganic substance determinations and biochemical determinations (col. 4, line 25 to col. 5, line 41). More particularly, within the category of inorganic substances that can be determined, the reference provides as an example, cations and anions such as aluminum, and specifically refers to indicators such as alizarinsulphonic acid, aurin tricarboxylic acid, Chromazurol S, Eriochrome cyanin or 8-

hydroxyquinoline (col. 4, lines 25-30). Within the category of diagnostic and biochemical determinations, the reference provides as an example, the determination of creatinine, and specifically refers to picric acid as an indicator (col. 5, line 21).

It is clear from the above description that the reference merely describes the use of conventionally known indicators for a given substance to be detected, and is far from recognizing the use of Chromazurol S or Eriochrome cyanine for the detection of creatinine. Specifically, the reference merely teaches the use of a conventionally used chemical method for the detection of creatinine with their invention, and in particular, the Jaffe method for the determination of creatinine.

On the other hand, Applicants have found for the first time that the properties of the compound expressed by formula (1) required by claim 1 are such that in the absence of creatinine, the compound reacts with Pd(II) to produce a colored complex, and in the presence of creatinine, the formation of the colored complex is inhibited by creatinine (see page 3, lines 2-7 of the specification). Advantageously, the test piece required by claim 1 avoids the serious problem of the liquid waste treatment involved with conventionally used chemical methods such as the Jaffe method, as strong alkaline reagents are not used, and does not involve the use of expensive enzymes or require a special facility for microdeterminations as in the enzymatic method (see page 1, line 36 to page 2, line 8 of the specification). Nothing in Fischer teaches or suggests using the compound expressed by the formula (1) for the measurement of creatinine as required by claim 1, let alone including the transitional metal along with the formula (1) in the test piece as required by claim 1.

The rejection notes that Pugia teaches a creatinine assay using cupric salt, and contends that it would have been obvious to use soluble cupric salt with the test kit of Fischer in the measurement of creatinine to form a colored complex with the indicator as motivated by Pugia to obtain the advantage of allowing the measurement to be conducted at neutral pH rather than high pH. Applicants respectfully contend that the rejection improperly uses hindsight in assessing the relevance of the reference.

Pugia teaches creatinine measurement by an enzymatic method, and distinguishes their method from conventionally used chemical methods such as the Jaffe method by indicating that their method does not use strong basic substances, which causes the absorbent carrier such as

porous films to become brittle (col. 1, line 60 to col. 2, line 5). In particular, Pugia's enzymatic method involves contacting a medium suspected of containing creatinine with cupric ions in the presence of a hydroperoxide and a redox indicator (col. 2, lines 25-30). Pugia notes that their invention is predicated on the discovery that a copper ion and creatinine are able to form a complex which will act as a pseudoperoxidase in the previously described system (the assay system to determine glucose in urine as described in col. 1, lines 17-30) in which the hydroperoxide in the presence of a peroxidase or pseudoperoxidase oxidizes the indicator to provide a detectable response (col. 2, lines 7-13). Pugia teaches that suitable oxidizable indicators include conventionally known oxidizable dye compounds, for example, benzidine; o-tolidine; a 3,3',5,5'-tetraalkylbenzidine wherein the alkyl group includes from one to about six carbon atoms; o-dianisidine; 2,7-diaminofluorene; bis-(N-ethylquinol-2-one)-azine; (N-methylbenzthiazol-2-one)-(1-ethyl-3-phenyl-5-methyltriazol-2-one)-azine or combinations thereof (col. 3, lines 58-64 and col. 1, lines 23-24). Pugia further teaches that the indicator becomes colored in the oxidized state (col. 1, lines 23-26), and that the copper forms a complex with creatinine to catalyze the interaction between the hydrogen peroxide and the indicator (col. 2, lines 8-13). The reference illustrates a possible set of reactions that includes the equilibrium reaction of the complex formation between the copper and the substance to be determined, namely creatinine (col. 2, lines 45-55), and there is no experimental work or detailed explanation that would lead one to a testing system in which the copper binds with the indicator, as opposed to the substance to be determined, to form a copper-indicator complex. Furthermore, as indicated above, Fischer teaches using the conventional chemical method for the detection of creatinine, and provides no reason to use Chromazurol S or Eriochrome cyanine for the detection of creatinine. Accordingly, contrary to the rejection's position, nothing in the references provides any reasonable basis for combining the soluble cupric salt of Pugia with the test kit of Fischer in the measurement of creatinine to form a complex with an indicator, let alone a colored complex with Chromazurol S or Eriochrome cyanine. Therefore, claim 1 and the dependent claims are patentable over the references for at least these reasons.

Moreover, claim 1 requires the use of Pd(II) as opposed to a cupric salt. Nothing in the references teaches or suggests including Pd(II) in a test piece for the measurement of creatinine

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as required by claim 1. Therefore, claim 1 and dependent claims are further removed from the references for these reasons.

As to claim 8, Fischer teaches that the material from which the moldings are made must be of such nature that no reagents are absorbed therein or held fast thereto (col. 3, lines 13-15). Fischer further notes that non-absorbent refers to inter alia to non-absorption of the embedded reagents, and distinguishes their support from the prior art by noting that absorbent supports, such as are customarily used for reagent strips, cannot be used (col. 3, lines 16-19). Pugia indicates that conventionally used absorbent supports include porous films (col. 1, lines 63-65). Therefore, contrary to the rejection's position, nothing in the references teaches or suggests including the compound expressed as formula (1) in a porous material as required by claim 8. Accordingly, claim 8 is further removed from the references for at least these reasons.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. Box 2902
Minneapolis, MN 55402-0902
(612) 455-3800

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By: _____
Douglas P. Mueller
Reg. No. 30,300
612.455.3800